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Review Article

LOCAL DRUG DELIVERY SYSTEMS IN THE TREATMENT OF PERIODONTITIS – AN OVERVIEW

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ABSTRACT

Periodontal diseases are chronic inflammatory disease in which microbial factors, host factors, environmental and genetic factors play a significant role in causing the disease. In that dental plaque is considered as the primary etiologic agent and it exists in a state of bio film. Plaque contains microorganisms which provoke inflammatory reaction from the host leading to connective tissue destruction, pocket formation and bone loss. Treatment options include surgical and non-surgical periodontal therapy. For mild to moderate periodontitis non-surgical methods are preferred. Non-surgical methods include scaling, root planing and anti-microbial therapy. Since periodontal pathogens reside inside the tissues, use of antimicrobials as adjunct to scaling and root planing is highly recommended. Antimicrobials can be delivered locally and systemically. Use of local drug delivery systems for treating periodontitis offers several advantages. This article discusses the various anti microbials used in treating periodontitis which are delivered as local drug delivery agent.

Keywords: Periodontitis, Dental plaque, Antimicrobials, Local drug delivery.

INTRODUCTION

Periodontal diseases are poly microbial infection affecting the supporting tissues of the teeth. Dental plaque is considered as the primary etiological agent for causing periodontal disease[1]. Plaque exists in a state of biofilm where microbes live as community instead of planktonic state. Biofilm environment provides nutrition and protection to the microorganisms[2]. Since tooth surface is a non-shedding surface, plaque accumulation if left unchecked progress to a mature form where gram negative organisms are more in number and they use early colonizers as receptors for attachment. Hence mechanical disruption of biofilms is necessary to maintain optimal oral health. Certain bacteria like Aggregatibacter actinomycetemcomitans have the potential to penetrate the connective tissues and reside there. Hence use of antimicrobials along with scaling and root planing is very much needed to eradicate the tissue associated bacteria [3,4,5,6].

Antimicrobials can be used both systemically as well as locally. Locally delivered antimicrobials offer several advantages than systemic antimicrobials.Locally delivered drugs does not produce systemic toxicity because these drugs are not absorbed into the systemic circulation. Resistance is not developed against locally delivered drugs and high concentration is maintained for longer period [7, 8].

Factors Affecting Local Delivery of Agents in Periodontal Pockets

A pharmacological agent must reach its site of action and be maintained there at a sufficient concentration for a sufficient time for an effect to occur and these three criteria affect the local delivery of agents to the periodontal pocket.

Site of Action

Targets for these agents are bacteria residing in periodontal pocket and those in junctional epithelium, connective tissue, cementum and dentine. Whatever agents we apply no only reach the pocket but also target the bacteria. Bio film environment needs to be disturbed for early penetration of local agent. Otherwise biofilm will prevent the agent from diffusing into the soft tissue wall.

Concentration

Drug should have a dose higher than Minimal Inhibitory Concentration (MIC). It is the in vitro concentration of drug that inhibits or kills 90% of target organisms in culture. The dose which cause side effect should be evaluated and therapeutic dose should be between MIC and toxic dose.

Time

Once a drug reaches the site of action in an effective concentration, it must remain at the site enough for its pharmacological effect to occur. In periodontal pocket biofilm environment causes slow growth of organism and it affect the effectiveness of antibiotics.

GCF clearance is very high. Drug concentration will be affected by this. Drug kinetics should follow zero order to stay there for long time.

Zero Order Reaction

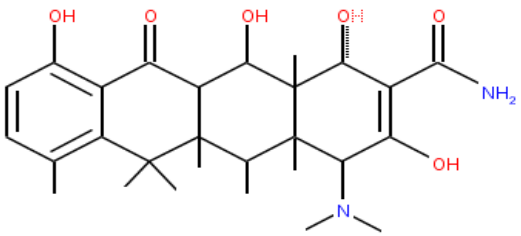
Constant amount of drug is excreted per unit of time

First Order Reaction

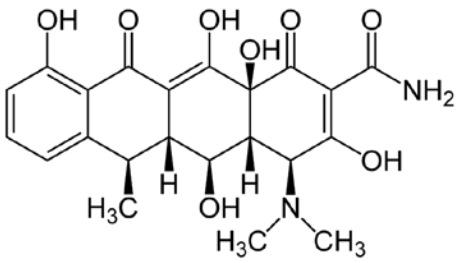
Constant fraction of drug is excreted per unit of time

If any drug follows zero order reaction the amount of drug will be retained in that place for long time. Hence drugs follow zero order reaction is used in local drug delivery system[9].

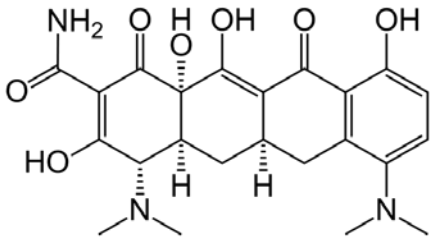
Drugs Used In Local Drug Delivery System



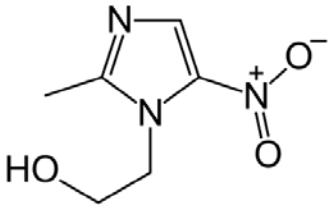
Tetracycline



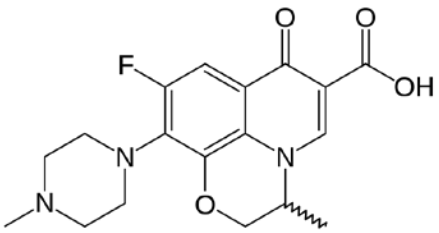
Doxycycline



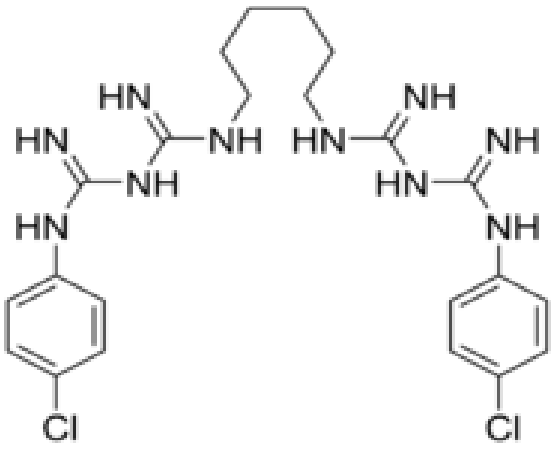
Minocycline



Metronidazole



Ofloxacin



Chlorhexidine

Mode of Delivery

Fibers, gel, microspheres and chip.

Slow release gel

2% minocycline – dentomycin

25% metronidazole – elyzol

Slow release fibres

Drug filled hollow fibers

Ethylene vinyl acetate co polymers (EVA)

Actisite

A monolithic fiber of EVA with diameter of 0.5mm containing 25% tetracycline is commercially marketed as actisite. Concentration 1590µg/ml is maintained for 10 days. This concentration is well above that necessary to inhibit the growth of all the susceptible bacterial species including those suspected as being periodontal pathogens.

The end of the fibre is first applied with a flat plastic instrument into pocket and successive layers are then packed wrapping the fibre around the tooth, so that all the sub gingival areas are filled. Excess fibre is trimmed with scissors and gingival margins sealed with cyanoacrylate adhesive.

Time taken: 5-15 min per tooth. Fibre left for 10days after which it is removed by scaler. Pockets will be dilated and root surface can be accessed clearly. Sub gingival scaling should be done and repacking for facilitating scaling.

EVA – 25% tetracycline fiber

Serum concentration is 0.1µg/ml and mean tetracycline concentration in tissue is 64ng/mg.

Root penetration of tetracycline is 10µm. MIC is 1-128µg/ml

Resistance is not reported in local drug delivery of tetracycline. The potential causes are:

- Concentration is maintained for 10days
- Drug is absorbed into gingival tissue to kill tissue associated bacteria
- No systemic absorption to alter the systemic flora

Microbes reduced in number are:

F.nucleatum, P.gingivalis, P.intermedia, C.rectus and A.actinomycetemcomitans

Indications

- Deep pockets with difficult access to scaling and root planing
- Deep pockets that fail to respond scaling
- Refractory sites
- Pockets exuding pus
- Sites with acute lateral abscess

Review of Literature

Tetracycline

In a study conducted to assess the clinical and microbiological effects of a newly developed root conditioning gel system containingtetracycline or a mixture of tetracycline and citricacid on non-surgicalperiodontaltherapy, sixty-four (64) single-rooted teeth with a probing depth of 4 to 6 mm were randomly subjected to one of the following four treatments; 1) root planing alone (RP group); 2) tetracycline-containinggel alone (TCG group); 3) root planing plus tetracycline-containing gel (RP + TCG group); or 4) root planing plus a mixture of tetracycline and citricacid-containinggel (RP + TC-CAG group). Probing depth, attachment level, and tooth mobility were measured and the presence of dental plaque and gingival inflammation was recorded at baseline and after 2, 4, 8, and 12 weeks. Subgingival plaque samples from each site were collected at the same visits and examined with phase contrast microscopy for proportions of motile rods and spirochetes. Plaque index, gingival sulcus bleeding index (SBI), probing depth, and attachment level decreased significantly in all groups compared to the baseline values. A significant decrease in probing pocket depth was noted after 12 weeks in RP + TC-CAG group compared to the other groups. Significantly more gain in attachment was detected in the RP + TC-CAG group compared to the TCG group. Tooth mobility scores also decreased later in the study. A significant decrease in the proportion of motile rods was found primarily in the RP + TC-CAG group[10].

A randomized single-blind multicentercontrolled clinical trial was conducted to clinically evaluate the effectiveness of adjunctive local controlled drug delivery in the control of bleeding on probing in mandibular class II furcations during maintenance care. 127 patients presenting with a classIImandibular furcation with bleeding on probing were included in the study. They had been previously treated for periodontitis and were participating in supportive care programs in periodontal specialty practices. Treatments consisted of scaling and root planing with oral hygiene instructions (control) and scaling and root planing and oral hygiene combined with local controlled drug delivery with tetracyclinefibers (test). The following outcomes were evaluated at baseline and 3 and 6 months after therapy at the furcation site: bleeding on controlled force probing (BOP), probing pocket depth (PD) and clinical attachment levels (CAL). Levels of oral hygiene and smoking status were also assessed. Both test and controls resulted in significant improvements of BOP and PD at 3 and 6 months. The test treatment resulted in a 0.5 mm greater reduction of PD than the control at 3 months, the improvement was highly significant but its duration did not extend until the 6 months evaluation. No differences were observed in terms of changes in CAL. These data indicate that addition of tetracyclinefibers to mechanical therapy alone resulted in improved control of periodontal parameters during periodontal maintenance of class II mandibular furcations. Short duration of the effect, however, requires further investigations to optimize conservative treatment of these challenging defects[11].

In a study, 46 upper and lower molars with furcation grade II involvement were selected from 16 patients with periodontal disease. The teeth were randomly allocated to the following groups according to treatment; (1) 4 consecutive administrations of tetracycline-immobilized cross-linked collagenfilm (TC film) at intervals of 1 week (TC group); (2) 1 root planing treatment (RP group); (3) combination treatment (TC + RP group); (4) no treatment (control group). The therapeuticeffects of each treatment were compared both clinically and microbiologically. Records of

plaque index, gingival index, bleeding on probing, probing depth, probing attachment level and microscopic counts were obtained at 0, 4, 6 and 8 weeks. The results showed marked decreases in probing depth and density of micro-organisms in both the RP and TC + RP groups. In particular, the TC + RP group was characterized by a decreased rate of bleeding on pocket probing and an increased probing attachment gain. The above findings demonstrated that rootplanning is effective in the treatment of furcation involvement and that the effects are enhanced by the local administration of TC films[12].

A study was conducted to compare the clinical effects of subgingivally placed 1% chlorhexidine gel (w/w) and 40% tetracycline (w/w) paste in periodontal pockets of 22 adult periodontitispatients. The 2 agents were applied following scaling and root planing in pockets exceeding 4 mm. The patients were randomly divided into 3 groups: (a) scaling and root planing (SCRP) only, the control group; (b) corsodylgel+SCRP; (c) Tetracyclinepaste+SCRP. Gel or paste was gently applied using a syringe with a blunt needle until the selected pocket was overfilled. Evaluations were made of clinicalparameters including the plaque index (PI), gingival index (GI), bleeding index (GI-S), probing pocket depths, probing attachment levels and position of the gingival margin. The results suggested that all the treatment modalities were effective in producing statistically significant improvements in clinicalparameters. It was concluded that the conventional treatment modalities were essential in the treatment of periodontal diseases, but in view of the structure of the periodontal pocket and adjacent complex root surface, subgingival drug application in certain cases, might also provide adjunctive improvement[13].

A clinical trial was conducted to compare the efficacy of scaling and root planing (S and RP) alone versus tetracyclinefibertherapy used adjunctively with S and RP in the treatment of localized recurrent periodontitis sites in maintenance patients. A total of 113 patients receiving regular supportive periodontal therapy (SPT) were treated with whole mouth S and RP. Two non-adjacent sites in separate quadrants were selected in each patient for monitoring based on criteria that the sites were 5 to 8 mm deep and had a history of bleeding on probing. The chosen sites were randomly assigned to one of the two treatment groups. Probing depth (PD), bleeding on probing (BOP), and clinical attachment level (CAL) were measured at baseline and 1, 3, and 6 months. At 1, 3 and 6 months, adjunctivefibertherapy was significantly better in reducing PD and reducing BOP than S and RP alone. At 6 months, fibertherapy was significantly better in promoting clinical attachment gain than S and RP alone. Overall, these results indicate that fibertherapy significantly enhanced the effectiveness of S and RP in the management of localized recurrent periodontitis sites, in patients receiving regular supportive periodontal treatment[14].

A 6-month follow-up parallel study was conducted to evaluate the efficacy of three commercially available local delivery systems as adjuncts to scaling and root planing in the treatment of sites with persistentperiodontal lesions. Seventy-nine patients with 4 pockets> or = 5 mm and bleeding on probing and/or suppuration were randomized into 4 treatment groups which included: scaling and root planing alone (S) (20 patients), or in conjunction with the application of 25% tetracycline fibers (S+Tet) (19 patients), or 2% minocycline gel (S+Min) (21 patients), or 25% metronidazole gel (S+Met) (19 patients). Clinical measurements were taken at baseline, 6 weeks, 3 months, and 6 months after antimicrobial application. All 4 therapies resulted in significant improvements from baseline in probing depth, attachment level, bleeding on probing, and the Modified Gingival Index (MGI) scores. The improvements in clinical parameters were greater in all 3 adjunctive treatment groups than scaling and root planing alone. The probing depth reduction at all time points was significantly greater in the scaling plus tetracycline fiber group than the scaling and root planing alone group (P<0.01). There was also a significant improvement for scaling plus tetracycline fiber application over scaling and metronidazole at both 6 weeks and 3 months, although this did not remain significant at the 6-month visit. While the frequency of sites with suppuration was markedly reduced following all antimicrobial treatments, the most effective reductions were seen in the scaling plus tetracycline fiber group, followed by the minocycline group. Although all 3 locally applied antimicrobial systems seem to offer some benefit over scaling and root planing alone, a treatment regimen of scaling and root planing plus tetracycline fiber placement gave the greatest reduction in probing depth over the 6 months after treatment[15].

A clinical study evaluated the influence of scaling and roots planning (SRP), with and without the use of tetracycline-loaded bovine absorbentmembrane, in the reduction of periodontalpockets according to 3 parameters: probing pocket depth (PPD), bleeding on probing (BOP) and plaque index (PI). Twenty-four patients were selected totalizing 144 random teeth divided in 2 groups (n=72 teeth) - control (SRP) and experimental (SRP with tetracycline-loadedabsorbentmembrane). PPD, BOP and PI were determined before and 28 days after the treatment. In all patients, the PPD values at the end of the treatment were always lower than the baseline values. There was a reduction of the PI for both treatments, but it was more evident on the experimental group. In conclusion, the use of tetracycline-loadedabsorbentmembrane could result in a better prognosis compared to scaling and root planning after only 28 days of evaluation[16].

Doxycycline

A study was conducted to evaluate the clinical effect of topical application of doxycyclineadjunctive to non-surgicalperiodontaltherapy. A total of 111 patients suffering from untreated or recurrent moderate to severe periodontitis were treated in this double-blind split-mouth study. In each patient, 3 different treatment modalities were assigned randomly to 3 test teeth: scaling and root planing alone (SRP), SRP with sub gingival vehicle control (VEH), and SRP with sub gingival application of a newly developed biodegradable 15% doxycycline gel (DOXI). At baseline, clinical parameters were measured at all single rooted teeth using a reference splint: PII, PPD, relative attachment level (RAL-V), GI. 3 strata were generated according to baseline PPD: (i) 5-6 mm, (ii) 7-8 mm, (iii) > or =9 mm. Not more than 50% active smokers were allowed to each stratum. 3 and 6 months after therapy re-examination was performed by examiners blinded to baseline data and test sites. DOXI provided statistically significantly more favorable PPD reduction and RAL-V gain than SRP and VEH after 6 months. Thus the study concluded that, adjunctive topical sub gingival application of a biodegradable 15% doxycycline gel was safe and provided more favorable RAL-V gain and PPD reduction than SRP alone and VEH[17].

A study was conducted to compare the effect of tooth related and patient related factors on the success of non-surgical and surgicalperiodontaltherapy. In 41 patients (22 female) with untreated and/or recurrent periodontitis, no therapy, scaling and root planing (SRP), or access flap (AF) were assigned according to probing pocket depth (PPD). PPD and vertical relative attachment level (RAL-V) were obtained initially, 3 and 6 months after therapy. Baseline data were compared according to therapy, jaw, tooth type, and site. Factors influencing clinical parameters were identified using multilevel analyses. Baseline PPDs were deeper inter proximally, in the maxilla and at premolars compared to buccal/oral sites, mandibular and anterior teeth. At 6 months, PPD reduction and RAL-V gain were significantly greater at sites receiving SRP and AF as compared to untreated sites ($p < 0.001$). PPD reduction and RAL-V gain were significantly less ($p < 0.005$) in smokers as compared to non smokers and at inter proximal sites ($p < 0.0001$) as compared to buccal/oral sites. RAL-V gain was less in aggressive periodontitis, and PPD reduction was less in the maxilla ($p < 0.001$). In sites with greater bone loss and infrabony defects, a poorer response was observed regarding RAL-V gain or PPD reduction, respectively. The conclusions of the study are the following: (1) Nonsurgical and surgicalperiodontal therapies are effective in single-rootedteeth; (2) severe interproximal bone loss and infrabony defects deteriorate clinical results; and (3) there seem to be more defect-associated (tooth, site) factors influencing treatment outcome than patient-associated factors[18].

A clinical study was conducted evaluate the clinical outcome of non-surgical retreatment at molar furcationsites by ultrasonic

debridement with or without adjunctive application of locally delivered doxycycline, and to explore factors affecting the healing results. This study involves 32 patients with chronic periodontitis, who received initial pocket/root debridement by ultrasonic instrumentation, followed by random assignment to retreatment of remaining pathologic sites at 3 months by ultrasonic instrumentation with or without adjunctive local application of an 8.8% doxycycline gel. Clinical examinations of plaque, probing depth (PD), relative attachment level, furcation involvement, and bleeding after furcation probing were performed initially, before retreatment at 3 months (baseline), and 3 and 9 months after retreatment. The primary efficacy variable was reduction in the degree of furcation involvement. A multilevel logistic model was used to evaluate the impact of patient and tooth site related factors on the main outcome variable. The retreatment including locallydelivereddoxycycline resulted in closure of 50% of degree I furcationsites, compared to 29% for sites treated with mechanical debridement only. Of the degree II furcationsites, 17% in the test and 11% in the control group were reduced in depth. The logistic multilevel model with "furcation improvement" as the dichotomous outcome variable revealed that local application of doxycycline had no statistically significant effect. Improvement in molar furcation involvement after non-surgical periodontal therapy was not enhanced by adjunctive locally applied doxycycline and negatively affected by increased vertical PD and tobacco smoking[19].

Minocycline

A study was conducted to investigate the association between the antimicrobial and clinical efficacy of minocycline hydrochloride microspheres when used adjunctively with scaling and root planing. 127 subjects with moderate-to-advanced chronic periodontitis were randomly assigned to receive minocycline microspheres plus scaling and root planing (n = 62) or scaling and root planing alone (n = 65). Deoxyribose nucleic acid analysis and clinical data were obtained at baseline and 30 days after treatment. End points included changes in the mean sum of red complex bacteria, pocket depth, number of deep pockets, bleeding on probing, and clinical attachment level from baseline to day 30. Regression analysis determined the association between microbiological and clinical efficacy. Minocycline microspheres plus scaling and root planing reduced pocket depth, the number of deep pockets and bleeding on probing, and increased clinical attachment level significantly more than scaling and root planing alone. Comparing minocycline microspheres plus scaling and root planing with scaling and root planing alone, the number needed to treat for a 2 mm pocket depth reduction difference was 6.5. Pocket depth reduction correlated significantly with a decrease in the numbers and proportions of red complex bacteria. Minocycline microspheres significantly improved all clinical parameters compared to scaling and root planing alone. The addition of minocycline microspheres to scaling and root planing led to a greater reduction in the proportions and numbers of red complex bacteria. The reduction in pocket depth was significantly correlated with the reduction of the proportions and numbers of red complex bacteria. Additionally, there were statistically greater improvements in all clinical parameters examined[20].

A randomized, split-mouth, single-masked study was conducted to compare the efficacy of a gel and microspheres as drug-delivery systems in the treatment of periodontal disease. Microspheres were prepared, the release patterns of the microspheres and gel formulations were analyzed using an ultraviolet spectrophotometer, and particle shapes were studied under a scanning electron microscope. A split-mouth design was followed in which 30 potential sites were identified and divided into three groups: one control group and two groups in which microspheres or a gel was placed. Patients were recalled at 1, 3, 6, and 9 months. Clinical recordings included plaque index (PI), gingival index (GI), probing depth (PD), and relative attachment level (RAL) measurements; subgingival plaque was also obtained for microbiologic examination prior to and after therapy. Microspheres had a more sustained release and a high initial drug concentration. There was a significant improvement in the PI and GI in the initial 3 months. The results were statistically significant at P = 0.01. The mean PD scores among scores for the three groups at baseline and follow-up visits showed a reduction of 0.4 to 1 mm. The microbiologic parameters were also statistically significant. These data suggest that the type of delivery system could significantly influence the outcome of therapy[21].

Metronidazole

A study was performed to assess and compare the clinical healing and the microbiological findings following local application of metronidazole or tetracycline to augment subgingival scaling in previously untreated adult periodontitis sites. Eighteen patients with moderate to severe adult periodontitis at single-rooted teeth were selected. In each patient, 3 interproximal sites having comparable root anatomy, probing depth > or =5 mm and bleeding on probing were randomly assigned to 1 of 3 treatment groups: 1) two sessions of subgingival scaling and root planing; 2) similar to 1, with each treatment supplemented with a 25% metronidazole sustained release gel; 3) similar to 1 with each treatment supplemented with a 3% tetracycline ointment. The treatments were performed by 1 operator and the clinical variables probing depth, attachment level, and bleeding on probing were evaluated at baseline, 3 months and 6 months by a second blinded examiner. The microbiological findings were evaluated using a commercial test kit. The average probing depth reduction for the 3 groups at 6 months was 1.5 mm and the average gain of clinical attachment was 0.8 mm. There were no significant differences between the effects following topical application of the metronidazole gel or the tetracycline ointment. Scaling and root planing alone appeared as effective as the drug augmented regimens, although there was a weak but non-significant tendency for better results in sites treated with the antibiotic drugs. Actinobacillus actinomycetemcomitans was generally not detected; Prevotella intermedia was not significantly reduced, while Porphyromonas gingivalis was significantly reduced in all treatment groups. It was concluded that the augmentative effect of the metronidazole gel and the tetracycline ointment was comparable but small compared to scaling and root planing alone[22].

A study was carried out to investigate the effect of 2 applications of a metronidazole 25% dental gel as adjunctive therapy to subgingival scaling with root planing. 59 of the original collective of 64 patients with adult periodontitis were observed for a 9-month period. This randomised single-blind study was carried out in split-mouth design. Each patient had to have at least 2 pockets with a probing depth of > or =5 mm in each quadrant. The clinical parameters, pocket probing depth (PPD), attachment level (AL) and bleeding on probing (BOP), were recorded at all teeth on days 0, 91, 175 and 259; in addition, subgingival plaque samples taken from 45 patients were analysed by means of dark-field microscopy. Therapy comprised subgingival scaling and root planing (SRP) of all quadrants and additional application of metronidazole 25%, dental gel in 2 randomly selected quadrants (SRP+Metro). Treatment was confined to teeth with a baseline PPD of > or =5 mm. Average PPD and AL and the incidence of BOP were computed for all pockets with a baseline PPD of > or =5 mm, and the 2 methods compared. The main efficacy variable for evaluation of the 2 treatments was the difference in PPD on day 259. Comparison of the 2 treatments revealed a statistically significant improvement in the clinical parameters for both treatment methods over the study period. Between baseline and day 259, significant differences in PPD and BOP were observed between the 2 treatment groups. Evaluation according to different patient groups demonstrated significant advantages of the combined therapy in previously-untreated patients, especially in female probands. Dark-field microscopy revealed a shift in the bacterial flora towards "healthy conditions". The results show that only minor advantages are to be gained from the application of a metronidazole 25% dental gel as adjunctive therapy to subgingival scaling[23].

An investigation was conducted to evaluate the effect of local antibiotic therapy with metronidazole adjunctively to scaling and root planing (SRP) versus mechanical treatment alone. 30 maintenance-patients were included in this single-blind study. The subjects had to comply with the following criteria: 2 non-adjacent sites with a probing depth > or =6 mm with bleeding on probing in separate quadrants, no periodontal therapy within the last 3 months, and no antibiotic therapy within the last 6 months. After

randomization, the study sites were assigned to one of the following 2 treatments: SRP plus subgingival application of metronidazole 25% dental gel (Elyzol) 5x during 10 days (test site) or SRP alone (control site). Subgingival microbiological samples were taken prior to, and 21 days and 3 months after scaling. The samples were analyzed with a commercial chair-side ELISA (Evalusite) for Porphyromonas gingivalis, Prevotella intermedia and Actinobacillus actinomycetemcomitans. Probing pocket depth (PPD), attachment level (AL) and bleeding on probing (BOP) were recorded at baseline and 3 months later. PPD reduction and AL-gain were statistically significant ($p<0.001$) after both treatments. However, there were no statistically significant differences between them. The same observation was made for BOP. P. gingivalis was reduced significantly after both treatments without statistically significant differences. P. intermedia were reduced significantly only after SRP. A. actinomycetemcomitans was not reduced significantly after either treatment. In conclusion, the repeated local application of metronidazole as an adjunct to SRP and the mechanical treatment alone showed similar clinical and microbiological effects without statistically significant differences with the exception of P. intermedia[24].

The effect of topical application of a metronidazole gel (ELYZOL DENTAL GEL), and adjunctive therapy in the treatment of adult periodontitis was assessed clinically. A single, masked examiner performed clinical assessments. Fourteen patients were involved, each one received four different treatments including control, and the four treatments were randomly applied to at least one tooth in each quadrant for each patient in a comparative split-mouth design. Clinical examinations were carried out before treatment and 90 days after treatment. All patients had at least one tooth in each quadrant with probing pocket depth of > or = 5mm. The four treatment groups were: (I) One session of one hour of scaling and root planing, (II) metronidazole 25% dental gel (ELYZOL DENTAL GEL) applied on day 0 and day 7, (III) scaling adjunctive to metronidazole 25%, and (IV) No treatment. Instruction in oral hygiene was given to all subjects at base line examination. At the end of the study (day 90), all groups had statistically significant improvement in probing pocket depth, and in plaque and bleeding indices when compared to day 0. However, group III had statistically significantly greater improvement in probing pocket depth than groups I, II and IV. Both groups I and II had statistically significantly greater improvement in probing pocket depth than control group. On the other hand, both groups were not statistically significantly different from each other in probing pocket depth improvement. It is suggested that topical Elyzol treatment may improve periodontal health as well as subgingival scaling and root planning therapy, and adjunctive treatment could obtain an additional therapeutic effect[25].

Chlorhexidine

A study was conducted to investigate the effects of a simplifiedsystem of oralhygiene, comprising Bass brushing, scaling, root planing and subgingival irrigation using a pulsated monojetoral irrigator, in patients with chronicperiodontitis. After initial assessment, patients received scaling, root planing and instruction in Bass brushing and in use of a pulsated jet oral irrigator (Water Pik + Imax attachment) to irrigate sub gingivally. 11 patients with 262 approximal periodontal pockets used 0.02% chlorhexidine (CH) or a placebo as the irrigating solution once daily for 28 days. Plaque index (PlI), sulcus bleeding index (SBI), and probing pocket depth (PPD) were assessed on days 0, 28, 56 and 84. Within procedure comparisons for all groups showed that the regime was highly effective in reducing PlI, SBI and PPD, improvements being maintained at least until day 84. Between procedure comparisons showed that benefits were improved only marginally by the use of 0.02% CH as the irrigation fluid. The patients found the procedure pleasant and neither injury nor staining was noted during the study. It was concluded that this simplifiedoralhygienesystem was effective in reducing periodontal inflammation and pocket depth; although no significant added benefit with 0.02% CH was apparent. The technique may be useful in patients who cannot achieve high levels of routine mechanical oral hygiene, particularly interdentially[26].

The maxillary teeth of 10 patients with moderately advanced chronic periodontitis were treated in a split-mouth design study. The baseline examination included plaque and bleeding scores, probing depths and probing attachment levels. 2 sites in each quadrant were selected for dark-field microscopic analysis. Each quadrant was randomly assigned to test or control and instrumented with an ultrasonic scaler using either 0.02% chlorhexidine or water as the coolant. Measurements were repeated 2, 6 and 10 weeks later, together with additional plaque sampling. Ultrasonic instrumentation with either chlorhexidine or water was equally effective in reducing bleeding scores and improving probing attachment levels. 42% of chlorhexidine- and 38.7% of water-treated sites showed gains of 1 mm or more in clinical attachment. Mean reductions in probing depth were similar (0.9 mm chlorhexidine, and 0.8 mm water). At the final examination, the chlorhexidine-treated quadrants had significantly more sites with probing depths in the 1-3 mm category and less in the greater than 3 mm category than the control quadrants (P less than 0.05). Both treatments reduced the microscopic counts of motiles and spirochaetes, resulting in a subgingival microbiota consistent with periodontal health. The results indicate that chlorhexidine has a slight adjunctive effect in the reduction of pocket depth when used as a coolant during ultrasonic root planing for the treatment of chronic periodontitis[27].

The clinical and microbial effects of a single episode of simultaneous ultrasonic scaling and subgingival irrigation with chlorhexidine (CHX) were studied as a function of clinicalprobingdepth in patients with adult periodontitis. 60 patients were randomly assigned to receive subgingival irrigation under cavitation with either sterile water or 0.12% CHX delivered through the tip of an ultrasonically activated scaler as part of initial periodontal therapy in a double-blind study design. 3 periodontal sites were randomly selected for examination from each patient on the basis of clinicalprobingdepth, with 1 site being selected within each of the following ranges: 1-3 mm, 4-6 mm, and 7-9 mm. Pretreatment and post-treatment (days 14 and 28) clinical assessments included a plaque index (PI), gingival index (GI), and clinicalprobingdepth (CPD). Subgingival specimens also were collected from 1-3 mm and 4-6 mm sites on a random subset of patients (15 per group). Plaque counts of spirochetes and motile organisms were made by darkfield microscopy. Significant reductions in PI, GI, and CPD were observed among all sites within both treatment groups at 14 and 28 days post-treatment. CHX irrigation resulted in a significantly greater reduction in CPD than did water among sites initially probing 4-6 mm at both 14 and 28 days post-treatment (25% versus 13% and 31% versus 18%, respectively). Spirochete counts were modestly but non significantly reduced at 14 days post-treatment among sites 4-6 mm within both treatment groups. These results suggest that subgingival irrigation with CHX during ultrasonicscaling provides differential clinical benefits that are site-dependent[28].

A randomised, split-mouth, single-blind study was conducted to determine the efficacy of controlled-release delivery of chlorhexidine gluconate 2.5 mg (PerioChip) in patients with residual bleeding pockets (>5 mm) at least 3 months following oral hygiene and root debridement phase therapy. 26 patients (non-smokers) were screened and potential study sites identified. Clinical parameters recorded at baseline and all subsequent visits were plaque index (PI), pocket probing depth (PPD), bleeding index (BI) and clinical attachment level (CAL). All study sites were debrided using ultrasonic instrumentation. Perio Chips (PC) were placed in the selected sites of two quadrants (left or right) whilst identified sites in the remaining quadrants were left without adjunctive antimicrobial treatment. Clinical measurements were made at follow-up visits after 1, 3 and 6 months. Mean changes from baseline in PPD, BI and CAL were calculated with the patient as the experimental unit and comparability between the treatments was determined using t-tests. At baseline there were no significant differences between PC and control sites for mean PI, PD, BI or CAL. The mean (SE) reductions in PPD for PC and control treatments were: 0.47 (0.1), 0.46 (0.1); 0.76 (0.1), 0.55 (0.1); 0.78 (0.1), 0.45 (0.1) for months 1, 3 and 6 respectively. Only at month 6 did the difference between treatments approach statistical significance. Mean (SE) reductions in CAL over the same periods were: 0.17 (0.1),

0.04 (0.08); 0.38 (0.1), 0.21 (0.1); 0.43 (0.1), 0.15 (0.09) p=0.048. Mean (SE) reduction in BI between PC and control treatments only reached statistical significance at 6 months: 1.08 (0.1), 0.59 (0.1) p=0.05. These data suggest that Perio Chip is beneficial for patients on maintenance therapy although the benefit is not apparent until 6 months after placement[29].

The safety and efficacy of a degradable, subgingivally placed drug delivery system containing 2.5 mg chlorhexidine (CHX) were evaluated in a randomized, blinded, multi-centerstudy of 118 patients with moderate periodontitis. A split-mouth design was used to compare the treatment outcomes of scaling and root planing (SRP) alone with the combined use of SRP and the CHX in pockets with probing depths of 5 to 8 mm. The two maxillary quadrants were used for the two treatment arms of the study. Scaling and root planing was performed at baseline only, while the CHX was inserted both at baseline and at 3 months. Clinical and safety measurements including probing depth (PD), clinical attachment level (CAL), and bleeding on probing (BOP) as well as gingivitis, plaque, and staining indices were recorded at baseline, and at 1, 3, and 6 months. The average PD reduction in the CHX-treated sites was significantly greater than in the sites receiving SRP alone at both 3 and 6 months with a mean difference of 0.42 mm (P < or = 0.01) at 6 months. The reduction in CAL at the treated sites was greater than at the SRP sites, although the difference was statistically significant at the 6-month visit only. An analysis of patients with initial probing depths of 7 to 8 mm (n = 56) revealed a significantly greater reduction in PD and CAL in those pockets treated with CHX compared to SRP at both 3 and 6 months. The mean differences between test and control sites at 6 months were 0.71 mm and 0.56 mm PD and CAL respectively[30].

A study was conducted to evaluate clinically the effectiveness of a chlorhexidine gluconate chip in sites still showing signs of disease during periodontalmaintenancetherapy. Forty-two maintenance non-smoking patients (previously treated with non-surgical scaling and root planing [SRP]), presenting at least one probing depth (PD) of 5 to 8 mm, and bleeding on probing (BOP) at single-rooted teeth were assigned randomly to two groups: treated with a chlorhexidine gluconate chip (CHIP group) and treated with SRP (SRP group). Patients were assessed for plaque index, gingival index, BOP, PD, clinical attachment level (CAL), and gingival recession at baseline, 6 weeks, and 3 and 6 months. Both treatments resulted in improvements in all parameters evaluated. After 6 months, a reduction in PD of 2.64 +/- 0.02 mm and 2.12 +/- 0.02 mm was observed for CHIP and SRP groups, respectively. The observed gain in CAL was 2.19 +/- 0.87 mm and 2.07 +/- 1.53 mm for CHIP and SRP groups, respectively in deep pockets; PD reduction was 3.60 +/- 0.70 mm for CHIP group and 2.83 +/- 0.62 mm for SRP group. Both treatments were equally effective in periodontal health reestablishment in inflamed single-root sites of maintenance patients. However, for deep pockets, the chlorhexidine gluconate chip was more effective than SRP in reducing PD[31].

A study was to verify the influence of the extended use of chlorhexidine after one-stage full-mouth (FM) SRP in patients with chronic periodontitis on the clinical outcome after 3 months. Eighty-one patients with pockets > or =5 mm were treated by FM. All patients rinsed additionally with 0.2% chlorhexidine (CHX) twice daily over 3 months. Plaque index, bleeding on probing, probing depth (PD) and clinical attachment level (CAL) were recorded at baseline and after 1 and 3 months. Over 3 months of extended use of CHX mouth rinse afterSRP showed slightly but statistically significant better results[32].

CONCLUSION

Eradication of microorganisms from the periodontal pocket is the most important step in treating periodontitis. The limitations of mouth rinsing and irrigation have prompted research for the development of alternative delivery systems. Recently, advances in delivery technology have resulted in the controlled release of drugs. The requirements for treating periodontal disease include a means for targeting an anti-infective agent to infection sites and sustaining its localized concentration at effective levels for a sufficient time while concurrently evoking minimal or no side effects[33]. This article has discussed the various antimicrobials used as local drug delivery agent in treating periodontitis. From that following conclusions can be made: local drug delivery system is used effectively in controlling tissue associated bacteria, it eradicates the periodontal pathogens for several weeks, local drug delivery system is effective for treating single rooted teeth than multi rooted teeth and mode of treatment for shallow periodontal pockets and recurrent periodontal disease.

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